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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/715,166	11/17/2003	Ting-Dong Zhang	WAX017-185360C	4088

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EXAMINER	
PAK, JOHN D	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 10/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/715,166	ZHANG, TING-DONG	
	Examiner	Art Unit	
	JOHN PAK	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-12 and 15-28* is/are pending in the application.

4a) Of the above claim(s) *10,11,18-21 and 25-28* is/are withdrawn from consideration.

5)☒ Claim(s) *12,15 and 16* is/are allowed.

6)☒ Claim(s) *17 and 22-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/9/2006 has been entered.

At the outset, applicant is reminded of MPEP 706.07(h) and 37 CFR 1.145. "Applicant cannot file an RCE to obtain continued examination on the basis of claims that are independent and distinct from the claims previously claimed and examined as a matter of right (i.e. applicant cannot switch inventions)." MPEP 706.07(h). "Any newly submitted claims that are directed to an invention that is independent and distinct from the invention previously claimed will be withdrawn from consideration and not entered." Id. See also MPEP 802.01 for the meaning of "independent and distinct."

Newly submitted or newly amended claims are directed to an invention that is independent or distinct from the invention originally examined before the RCE for the following reasons:

I. Claims 10-11 and 18-21, directed to a method of treating leukemia in humans comprising utilizing a stabilized aqueous solution of 0.1-1.0 wt% arsenic trioxide to administer to a human as an intravenous drip.

II. Claims 25-26, directed to an intravenous solution comprising approximately 0.1-1 wt% arsenic trioxide, 0.8 wt% sodium chloride, and 10 wt% glucose. ** *Note, claim 26 incorrectly depends on claim 24. Placement of claim 26 in this group is based on the fact that claim 26 is directed to an intravenous solution.*

III. Claim 27, directed to a method of treating leukemia with an aqueous solution of arsenic trioxide, wherein there is (i) no claim-recited wt.% for arsenic trioxide, (ii) no other claim-recited solution ingredients, and (iii) no claim limitation to administer as an intravenous drip.

IV. Claim 28, directed to an aqueous solution comprising arsenic trioxide and at least one stabilizing agent, wherein there is no claim-recited percentage for arsenic trioxide and no identification of the stabilizing agent(s).

Previously examined claims and invention are most broadly represented by claim 12 in its original (pre-RCE) version, reproduced below.

> 12. (New) A method of treating leukemia in humans comprising the steps of:
>
> (a) preparing an aqueous solution consisting of approximately 0.1% to 1.0% by weight arsenic trioxide and at least one pH-buffering agent selected from the group consisting of hydrochloric acid, alkali hydroxide, and carbonate solutions;
>
> (b) sterilizing said aqueous solution to form an injectably administrable leukemia treating composition; and
>
> (c) administering said composition as an intravenous drip to a human in need of treatment for leukemia.

The originally examined claims did not require a stabilized aqueous solution or stabilizer. The originally examined claims required 0.1-10 wt% arsenic trioxide. The originally examined claims required administering the composition as an intravenous drip. The originally examined claims were directed to a method of treating leukemia with an intravenous drip, not the aqueous solution per se. The new or newly amended claims, as set forth above, are directed to independent or distinct inventions because they fail to require such inventive features.

First, the solution per se (inventions II and IV), whether or not it contains a stabilizer, is distinct from the originally claimed and examined method of treating leukemia. U.S. Patents 6,982,096, 6,884,439 and 6,770,304 are cited to establish that method of treating leukemia with arsenic trioxide is separate subject for patentability. A solution of arsenic trioxide can have materially different uses, such as in the treatment of breast cancer or controlling pests.

Second, it is known that arsenic can kill, cause cancer, or treat cancer. Given the dichotomy of arsenic as a "delicious poison" (Kwong et al., see IDS of 11/17/2003), the particular formulation or process of preparing a solution of arsenic trioxide will be material to patentability. The originally claimed and examined method of preparing and delivering the aqueous solution of arsenic trioxide is distinct for the differences noted above. In this art, even a slightly different method of delivering the same exact arsenic

trioxide for the same exact leukemia is considered separate subject for patentability. See e.g., U.S. Patent 6,884,439.

For these reasons, claims 10-11, 18-21 and 25-28 are directed to independent or distinct inventions. As a result, they cannot be examined in this RCE. See MPEP 706.07(h).

As for remaining claims 12, 15-17 and 22-24, they are deemed as being directed to an invention that is not distinct over the originally claimed and examined invention. Current version of independent claim 12 differs from the original version, but the two versions are close enough in that the current version does not require a stabilizer and the current version still recites 0.1-1 wt% arsenic trioxide and administration as an intravenous drip, wherein the HCl, alkali hydroxide and carbonate from the original version is now recited in dependent form as dependent claims 22-24.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits in this RCE. Accordingly, claims 10-11, 18-21 and 25-28 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 12, 15-17 and 22-24 will presently be examined.

The amendment filed on 11/9/2005 stands objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the inserted text (underlined in the marked up amendment) in the paragraph beginning on page 2 at line 23 and ending on page 3 at line 2. For ease of reference, the entire substitute paragraph of the amendment is reproduced below:

> The experimental results demonstrate that the intravenous composition of the present invention exert a strong abruptive effect on the membranes on cancer cells, such as leukemic cells. The intravenous composition of the present invention may also incorporate a pH-buffering agent in order to control the pH for effective and safe administration of the composition to patients. The pH-buffering agent is selected from the group consisting of hydrochloric acid (HCl), alkali hydroxide, such a sodium hydroxide, or carbonate solutions, as taught by Merck Index, 10th Ed: 1983, p. 117 (compound 824 - arsenic trioxide). It inhibits DNA/RNA synthesis and reduces the proliferation of the leukemic cells. The experiments, both *in vivo* and *in vitro* have demonstrated that the intravenous composition of the present invention is effective in destroying leukemic cells while inducing increased cell differentiation to produce normal cells. Additionally, the recovery of hematopoietic function is accelerated. It has also been found that the composition of the present invention can pass through the blood-brain barrier.

As explained before in the previous Office actions, the pH buffering feature does not find adequate descriptive support from the originally filed disclosure. Prior to applicant's

11/9/2005 amendment, there had never been a disclosure of a pH-buffering agent "for effective and safe administration of the composition to patients." Not once in any discussion or any examples is there any mention of a pH buffering agent. Applicant discloses on specification page 4, lines 14-19 that "The detailed procedure for the preparation of the composition comprises boiling 1000 ml of sterile water for injection, adding arsenic trioxide, boiling for a further 30 minutes until the arsenic trioxide is completely dissolved, adding sodium chloride and q.s. with water to 1000 ml." Even in the detailed procedure the originally filed disclosure failed to convey a pH buffering agent.

The amendatory subject matter is new matter. Applicant is required to cancel the new matter in the reply to this Office Action.

Applicant argues in the submission filed on 8/9/2006 that the added material above is an "inherent property of providing long term intravenous solutions to a human." This is an interesting interpretation of "may also incorporate" --

> cells. The intravenous composition of the present invention may also incorporate a pH-buffering agent in order to control the pH for effective and safe administration of the composition to patients. The pH-buffering agent is selected from the group consisting of hydrochloric acid

Applicant amended to disclose an optional incorporation of a pH buffering agent, as evidenced by "may also incorporate." An optional agent certainly does not present an "inherent property."

Applicant also argues that "[o]ne of ordinary skill in the art would recognize that the addition of a pH buffer in the Applicant's solution is necessary in order to avoid blood imbalance during the provision of intravenous solution over time." Applicant's arguments are simply not consistent with the facts of this case. First, applicant failed to originally disclose the pH buffering agent. Second, applicant failed to state in the 11/9/2005 amendment that buffering agent was required, i.e. not optional. Third, applicant's new claim 27, submitted with applicant's current arguments, is directed to treatment of leukemia with intravenous arsenic trioxide, which does not require a pH buffering agent. Given that numerous other claims positively recite a pH buffering agent, absence of the pH buffering agent in claim 27 is evidence that claim 27 does not require a pH buffering agent to treat leukemia with intravenous arsenic trioxide. Applicant's inherency arguments are therefore found unpersuasive.

It is noted that preliminary amendments to the claims and specification were filed on 11/17/2003. The filing date of this application is also 11/17/2003. For applications filed before 9/21/2004, preliminary amendments are **not** treated as part of the original disclosure. 37 CFCR 1.115. Therefore, applicant's preliminary amendments of 11/17/2003 cannot be treated as part of the original disclosure, because (1) this application was filed before the effective date (9/21/2004) of amended 37 CFR 1.115, and (2) the preliminary amendment was not referenced in the oath/declaration.

Claims 22-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Independent claims 22-24 require preparing an aqueous solution comprising of arsenic trioxide with excipients and a pH-buffering agent (broadly in claim 22), or a pH-buffering agent selected from the group consisting of hydrochloric acid, alkali hydroxide, and carbonate solutions (claims 23-24). There is absolutely no descriptive support for a pH buffering agent in general or the specific agents as a pH buffering agent.

Therefore, the originally filed disclosure failed to convey to the skilled artisan that the aqueous solution of arsenic trioxide is to also include at least one pH-buffering agent, such as one selected from the group consisting of hydrochloric acid, alkali hydroxide, and carbonate solutions. Disclosure in an application that merely renders the later-claimed (by amendment) invention obvious is not sufficient to meet the written description requirement of 35 USC 112, first paragraph. Lockwood v. American Airlines, 41 USPQ 2d 1961, 1966 (Fed. Cir. 1997). The claims thereby fail to comply with the written description requirement of 35 USC 112, first paragraph.

Applicant's arguments of 8/9/2006 have been given due consideration but they were deemed unpersuasive. Applicant relies on the arguments made with respect to

the objection to the specification (new matter objection). The Examiner has addressed those arguments previously in this Office action, and the discussion there is incorporated herein by reference. For the reasons previously stated, applicant's arguments are found unpersuasive.

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claim 17 is rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 2 of prior U.S. Patent No. 6,720,011. This is a double patenting rejection.

Patented claim 2 recites the same exact ingredients, method of preparing, method of administering, subjects, and duration of treatment. The only language difference in the claims is that instant claim 17, which depends on instant claim 12, does not expressly recite water as an ingredient of the prepared aqueous solution. However, instant claim 12 directs the preparation of an aqueous solution in step (a), which by definition has to contain water for it to be aqueous. Therefore, instant claim 17 is identical to patented claim 2.

Claims 12 and 15-16 are allowed. It is noted for the record that the invention of claims 12 and 15-16 is deemed an obvious variation of the invention set forth in claims 1-4 of U.S. Patent 6,720,011 (direct parent case to this case). However, because a terminal disclaimer over said Patent has already been filed in this application, no further action by the Examiner is warranted with respect to claims 12 and 15-16.

The IFW record of this case does not appear to have an initialed copy of applicant's IDS of 11/17/2003. All of the references were considered at the time of the first action on the merits – all of the references were previously cited in the parent application and considered again at the time of the first action on the merits. An initialed and signed copy of the PTO-1449 is provided herewith.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to JOHN PAK whose telephone number is **(571)272-0620.** The Examiner can normally be reached on Monday to Friday from 8 AM to 4:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's SPE, Johann Richter, can be reached on **(571)272-0646**.

The fax phone number for the organization where this application or proceeding is assigned is **(571)273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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